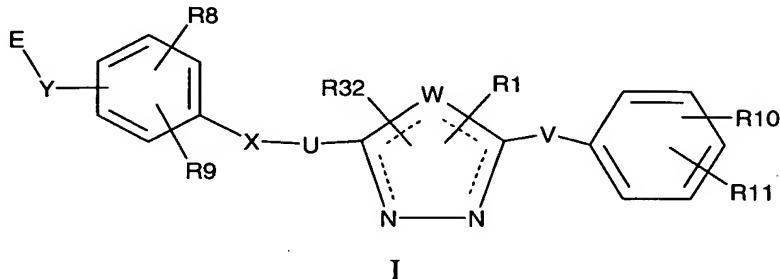


CLAIMS

(a) What is claimed is:

1. 1. (Withdrawn) A compound of the Formula I:



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

- (a) R1 is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₁-C₈ alkenyl, C₁-C₈ heteroalkyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl, and, wherein C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three substituents independently selected from R1';
- (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR12, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryloxy, aryl-C₀-4-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, OS(O)₂R16, N(R17)₂, NR18C(O)R19, NR20SO₂R21, SR22, S(O)R23, S(O)₂R24, and S(O)₂N(R25)₂; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;
- (c) V is selected from the group consisting of C₀-C₈ alkyl and C₁-6-heteroalkyl;
- (d) X is selected from the group consisting of a single bond, O, S, S(O)₂ and N;
- (e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;

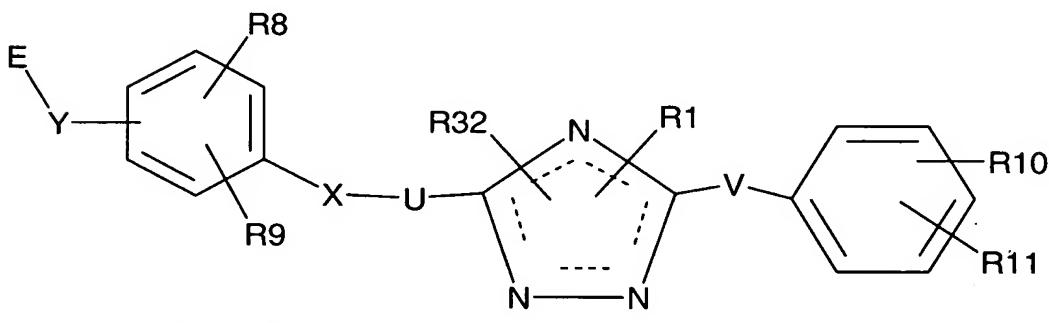
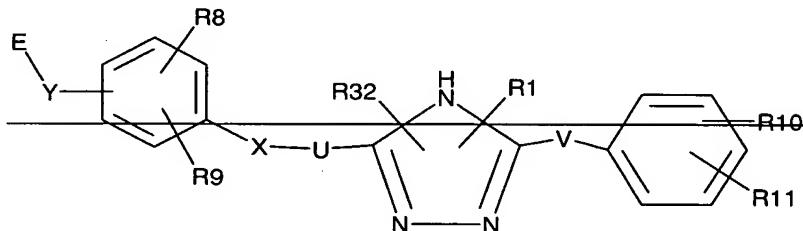
- (f) W is N, O or S;
- (g) Y is selected from the group consisting of C, O, S, NH, and a single bond;
- (h) E is C(R3)(R4)A or A and wherein
 - (i) A is selected from the group consisting of carboxyl, tetrazole, C₁-C₆ alkynitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R⁷;
 - (ii) each R⁷ is independently selected from the group consisting of hydrogen, C₁-C₆ haloalkyl, aryl C₀-C₄ alkyl and C₁-C₆ alkyl;
 - (iii) R3 is selected from the group consisting of hydrogen, C₁-C₅ alkyl, and C₁-C₅ alkoxy; and
 - (iv) R4 is selected from the group consisting of H, C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl, and aryl C₀-C₄ alkyl, and R3 and R4 are optionally combined to form a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with from one to three substituents each independently selected from R26;
- (i) R8 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, and halo;
- (j) R9 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, halo, aryl-C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, and OR29, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C₁-C₄ alkyl;
- (k) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkylenyl, C₁-C₆ alkyl-COOR12'', C₀-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)₂R16', N(R17')₂, NR18'C(O)R19', NR20'SO₂R21', SR22', S(O)R23', S(O)₂R24', and S(O)₂N(R25')₂; and wherein aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl are

each optionally substituted with from one to three independently selected from R28; and wherein R10 and R11 optionally combine to form a 5 to 6 membered fused bicyclic ring with the phenyl to which they are bound;

- (l) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;
- (m) R30 is selected from the group consisting of C₁-C₆ alkyl, aryl-C₀₋₄-alkyl, aryl- C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, and wherein C₁-C₆ alkyl, aryl-C₀₋₄-alkyl, aryl- C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;
- (n) R32 is selected from the group consisting of a bond, hydrogen, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, and C₁-C₆ alkyloxo; and
- (o) ---- is optionally a bond to form a double bond at the indicated position.

2. (Canceled)

3. (Currently Amended) A compound as claimed by Claim 1 wherein the compound is of the Formula Ic:



Ic

and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

- (a) R1 is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₁-C₈ alkenyl, C₁-C₈ heteroalkyl, aryl-C₀-₄-alkyl, aryl-C₁-₄-heteroalkyl, heteroaryl-C₀-₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀-₂-alkyl, and, wherein C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀-₄-alkyl, aryl-C₁-₄-heteroalkyl, heteroaryl-C₀-₄-alkyl, C₃-C₆ cycloalkylaryl-C₀-₂-alkyl are each optionally substituted with from one to three substituents independently selected from R1';
- (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR12, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryloxy, aryl-C₀-₄-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, OS(O)₂R16, N(R17)₂, NR18C(O)R19, NR20SO₂R21, SR22, S(O)R23, S(O)₂R24, and S(O)₂N(R25)₂; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;
- (c) V is selected from the group consisting of C₀-C₈ alkyl and C₁-₄-heteroalkyl;
- (d) X is selected from the group consisting of a single bond, O, S, S(O)₂ and N;
- (e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is substituted with from one to four substituents each independently selected from R30;
- (f) Y is selected from the group consisting of C, O, S, NH, and a single bond;
- (g) E is C(R3)(R4)A or A and wherein
 - (i) A is selected from the group consisting of carboxyl, tetrazole, C₁-C₆ alkynitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R⁷;
 - (ii) each R⁷ is independently selected from the group consisting of hydrogen, C₁-C₆ haloalkyl, aryl C₀-C₄ alkyl and C₁-C₆ alkyl;

- (iii) R3 is C₁-C₂ alkyl selected from the group consisting of hydrogen, C₁-C₅ alkyl, and C₁-C₅ alkoxy; and
- (iv) R4 is methyl selected from the group consisting of H, C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl, and aryl C₀-C₄ alkyl, and R3 and R4 are optionally combined to form a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl alkyl are each optionally substituted with from one to three substituents each independently selected from R26;
- (h) R8 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylene, and halo;
- (i) R9 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylene, halo, aryl-C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, and OR29, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C₁-C₄ alkyl;
- (j) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkylene, C₁-C₆ alkyl-COOR12'', C₀-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)₂R16', N(R17')₂, NR18'C(O)R19', NR20'SO₂R21', SR22', S(O)R23', S(O)₂R24', and S(O)₂N(R25')₂; and wherein aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three independently selected from R28; and wherein R10 and R11 optionally combine to form a 5 to 6 membered fused bicyclic ring with the phenyl to which they are bound;
- (k) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;
- (l) R30 is selected from the group consisting of C₁-C₆ alkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl, and wherein C₁-C₆ alkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl,

heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

- (m) R32 is selected from the group consisting of a bond, hydrogen, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, and C₁-C₆ alkyloxo; and
- (n) ---- is optionally a bond to form a double bond at the indicated position.

- 4. (Canceled)
- 5. (Canceled)
- 6. (Canceled)
- 7. (Canceled)
- 8. (Canceled)

9. (Currently Amended) A compound as claimed by Claim 3 ~~any one of Claims 1 through 8~~ wherein X is O.

10. (Currently Amended) A compound as claimed by ~~any one of Claims 1 through 8~~ Claim 3 wherein X is S.

11. (Currently Amended) A compound as claimed by Claim 3 ~~any one of Claims 1 through 10~~ wherein Y is O.

12. (Currently Amended) A compound as claimed by Claim 3 ~~Claim 9 any one of Claims 1 through 10~~ wherein Y is C.

13. (Currently Amended) A compound as claimed by Claim 3 ~~any one of Claims 1 through 10~~ wherein Y is S.

14. (Currently Amended) A compound as claimed by Claim 3 ~~any one of Claims 1 through 13~~ wherein two of “----” in the five membered ring are each a bond to form double bonds at the designated locations.

15. (Withdrawn) A compound as claimed by any one of Claims 1 through 14 wherein E is C(R3)(R4)A.

16. (Currently Amended) A compound as claimed by Claim 14 any one of Claims 1 through 15 wherein A is COOH.

17. (Currently Amended) A compound as claimed by Claim 16 any one of Claims 1 through 16 wherein R10 is haloalkyl.

18. (Original) A compound as claimed by Claim 17 wherein R10 is CF₃.

19. (Withdrawn) A compound as claimed by any one of Claims 1 through 16 wherein R10 is haloalkyloxy.

20. (Withdrawn) A compound as claimed by any one of Claims 1 through 16 wherein R10 and R11 are each independently selected from the group consisting of hydrogen, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR12'', C₁-C₆ alkoxy, C₁-C₆ haloalkyl, and C₁-C₆ haloalkyloxy.

21. (Currently Amended) A compound as claimed by Claim 14 any one of Claims 1 through 16 wherein R10 and R11 are each independently selected from the group consisting of C₁-C₂ alkyl.

22. (Withdrawn) A compound as claimed by any one of Claims 1 through 16 wherein R10 is selected from the group consisting of C₃-C₇ cycloalkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, and aryloxy.

23. (Currently Amended) A compound as claimed by Claim 14 any one of Claims 1 through 22 wherein R1 is optionally substituted C₂-C₃ arylalkyl.

24. (Currently Amended) A compound as claimed by Claim 14 any one of Claims 1 through 23, wherein R8 and R9 are each independently selected from the group consisting of hydrogen and C₁-C₃ alkyl.

25. (Withdrawn) A compound as claimed by any one of Claims 1 through 22 and 24 wherein R1, V, R3, and R4 are each independently selected from the group consisting of C₁-C₂ alkyl.

26. (Withdrawn) A compound as claimed by any one of Claims 1 through Claim 22 and 24 wherein R1, R3, and R4 are each independently selected from the group consisting of hydrogen and C₁-C₂ alkyl.

27. (Currently Amended) A compound as claimed by Claim 3 ~~any one of Claims 1 through 24 or Claim 26~~ wherein V is a bond.

28. (Currently Amended) A compound as claimed by Claim 14 ~~any one of Claims 1 through 24~~ wherein V is selected from the group consisting of C₀-C₁ alkyl.

29. (Currently Amended) A compound as claimed by Claim 14 ~~any one of Claims 1 through 28~~ wherein U is C₁-C₃ alkyl.

30. (Currently Amended) A compound as claimed by ~~any one of Claims 1 through 29~~ Claim 29 wherein U is saturated.

31. (Currently Amended) A compound as claimed by Claim 14 ~~any one of Claims 1 through 22 or 24 through 30~~ wherein R1 is C₁-C₆ heteroalkyl.

32. (Currently Amended) A compound as claimed by Claim 3 ~~any one of Claims 1 through 31~~ wherein one carbon of the aliphatic linker is replaced with an O.

33. (Currently Amended) A compound as claimed by Claim 14 ~~claimed by any one of Claims 1 through 31~~ wherein U is an aliphatic linker having one carbon replaced by N.

34. (Currently Amended) A compound as claimed by Claim 14 ~~any one of Claims 1 through 31~~ wherein U is an aliphatic linker having one carbon replaced by S.

35. (Currently Amended) A compound as claimed by Claim 30 any one of Claims 1 through 34 wherein the aliphatic linker is substituted with from one to three substituents each independently selected from R30.

36. (Original) A compound as claimed by Claim 35 wherein the aliphatic linker is substituted with from one to two substituents each independently selected from R30.

37. (Currently Amended) A compound as claimed by Claim 36 any one of Claims 1 through 36 wherein each R30 is independently selected from the group consisting of C1-C6 alkyl.

38. (Currently Amended) A compound as claimed by Claim 37 any one of Claims 1 through 37 wherein each R30 is independently selected from the group consisting of C2-C3 alkyl.

39. (Withdrawn) A compound as claimed by any one of Claims 1 through 36 wherein R30 is independently selected from the group consisting of aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C_{3-C6} cycloalkylaryl-C₀₋₂-alkyl.

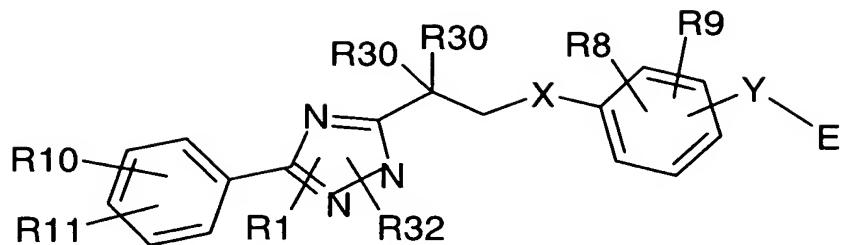
40. (Canceled)

41. (Currently Amended) A compound as claimed by Claim 37 any one of Claims 1 through 40 wherein U is substituted with methyl.

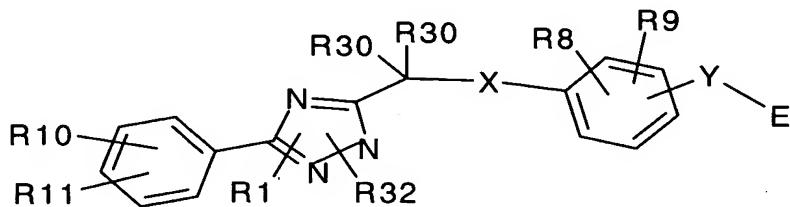
42. (Currently Amended) A compound as claimed by Claim 3 Claim 2 any one of Claims 1 through 41 wherein U is methylene.

43. (Currently Amended) A compound as claimed by Claim 3 any one of Claims 1 through 16 and 22 through 42 wherein R10 and R11 combine to form a fused 6 membered ring.

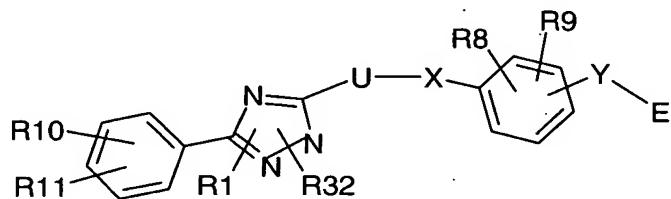
44. (Withdrawn) A compound as claimed by any one of Claims 1-3, 8-13, 15-24, 26, and 36-41 represented by the following Structural Formula IV:



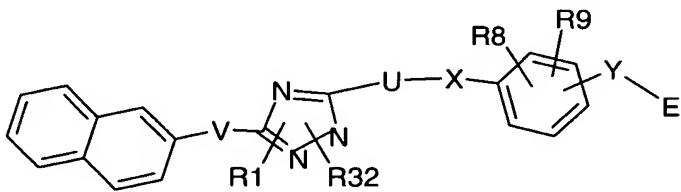
45. (Withdrawn) A compound as claimed by any one of Claims 1-3, 8-13, 15-24, 26, 36-41 represented by the following Structural Formula V:



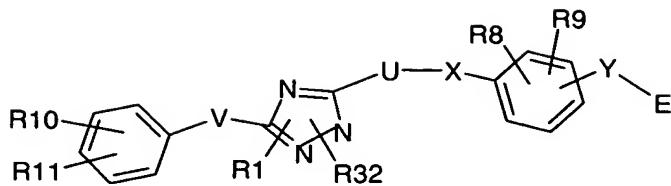
46. (Currently Amended) A compound as claimed by Claim 3 any one of Claims 1-3, 8-13, 15-24, 26, 36-41, represented by the following Structural Formula VI:



47. (Withdrawn) A compound as claimed by any one of Claims 1-3, 8-13, 15-24, 26, 36-41, represented by the following Structural Formula VIII:



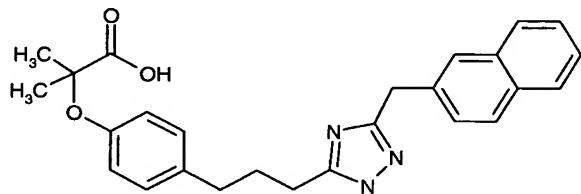
48. (Currently Amended) A compound as claimed by Claim 3 any one of Claims 1-3, 8-13, 15-24, 26, 36-41, represented by the following Structural Formula IX:



49. (Withdrawn) A compound as claimed by any one of Claims 1 through 48 wherein X and Y are substituted at a 1,4-position, such that X and Y are para substituted to one another.

50. (Withdrawn) A compound as claimed by any one of Claims 1 through 48 wherein X and Y are substituted at a 1,3-position, such that X and Y are meta substituted to one another.

51. (Currently Amended) A compound as claimed by Claim 3 any one of Claims 1 wherein the compound is a compound of the formula:



or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

52. (Currently Amended) A compound as claimed by Claim 3 any one of Claims 1 through 50 wherein X is a bond.

53. (Withdrawn) A compound as claimed by any one of Claim 1 which is 2-Methyl-2-{4-[3-(5-naphthalen-2-ylmethyl-2H-[1,2,4]triazol-3-yl)-phenoxy}proprionic acid.

54. (Withdrawn) A compound as claimed by any one of Claims 1 through 53 that is the S conformation.

55. (Withdrawn) A compound as claimed by any one of Claims 1 through 53 that is the R conformation.

56. (Currently Amended) A pharmaceutical composition, comprising as an active ingredient, at least one compound as claimed by Claim 3 ~~any one of Claims 1 through 55~~ together with a pharmaceutically acceptable carrier or diluent.

57. (Withdrawn) A method of modulating a peroxisome proliferator activated receptor, comprising the step of contacting the receptor with at least one compound as claimed by any one of Claims 1 through 55.

58. (Currently Amended) A method for treating diabetes mellitus in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claim 3~~Claim 1~~~~Claims 1 through 55~~.

59. (Currently Amended) A method for treating metabolic disorder in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claim 3~~Claims 1 through 55~~.

60. (Original) A method of Claim 59 wherein the mammal in need thereof is diagnosed as suffering from metabolic disorder.

61. (Withdrawn) A method for selectively modulating a PPAR delta receptor comprising administering a compound as claimed by any one of Claims 1 through 55 to a mammal in need thereof.

62. (Withdrawn) The manufacture of a medicament for use in the treatment and/or prevention of a metabolic disorder, wherein the compound is a compound as claimed by any one of Claims 1 through 55.

63. (Currently Amended) A method for treating atherosclerosis in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound of Claim 3~~Claims 1 through 55~~.

64. (Currently Amended) A compound as Claimed by Claim 3~~any one of Claims 1 through 55~~ for use as a pharmaceutical.

65. (Currently Amended) A method for treating or preventing the progression of cardiovascular disease in a mammal in need thereof comprising administering a therapeutically effective amount of at least one compound as Claimed by Claim 3 Claim 1 any one of Claims 1 through 55.

66. (Original) A method as claimed by Claim 65 wherein the mammal is diagnosed as being in need of such treatment.

67. (Withdrawn) A compound as claimed by any one of Claims 1 through 55 wherein the compound is radiolabeled.

68. (Withdrawn) A compound as disclosed by any one of the Examples herein.

69. (Withdrawn) All methods disclosed herein of preparing the compounds represented by Structural Formula I.

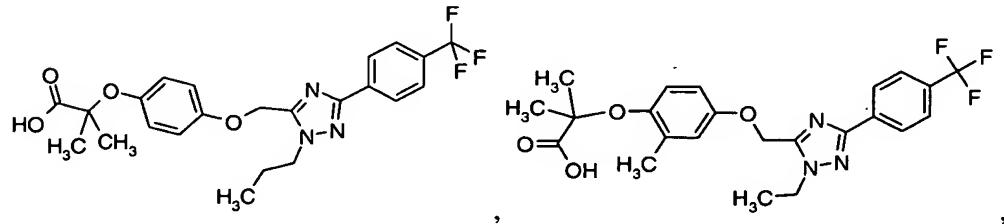
70. (Canceled)

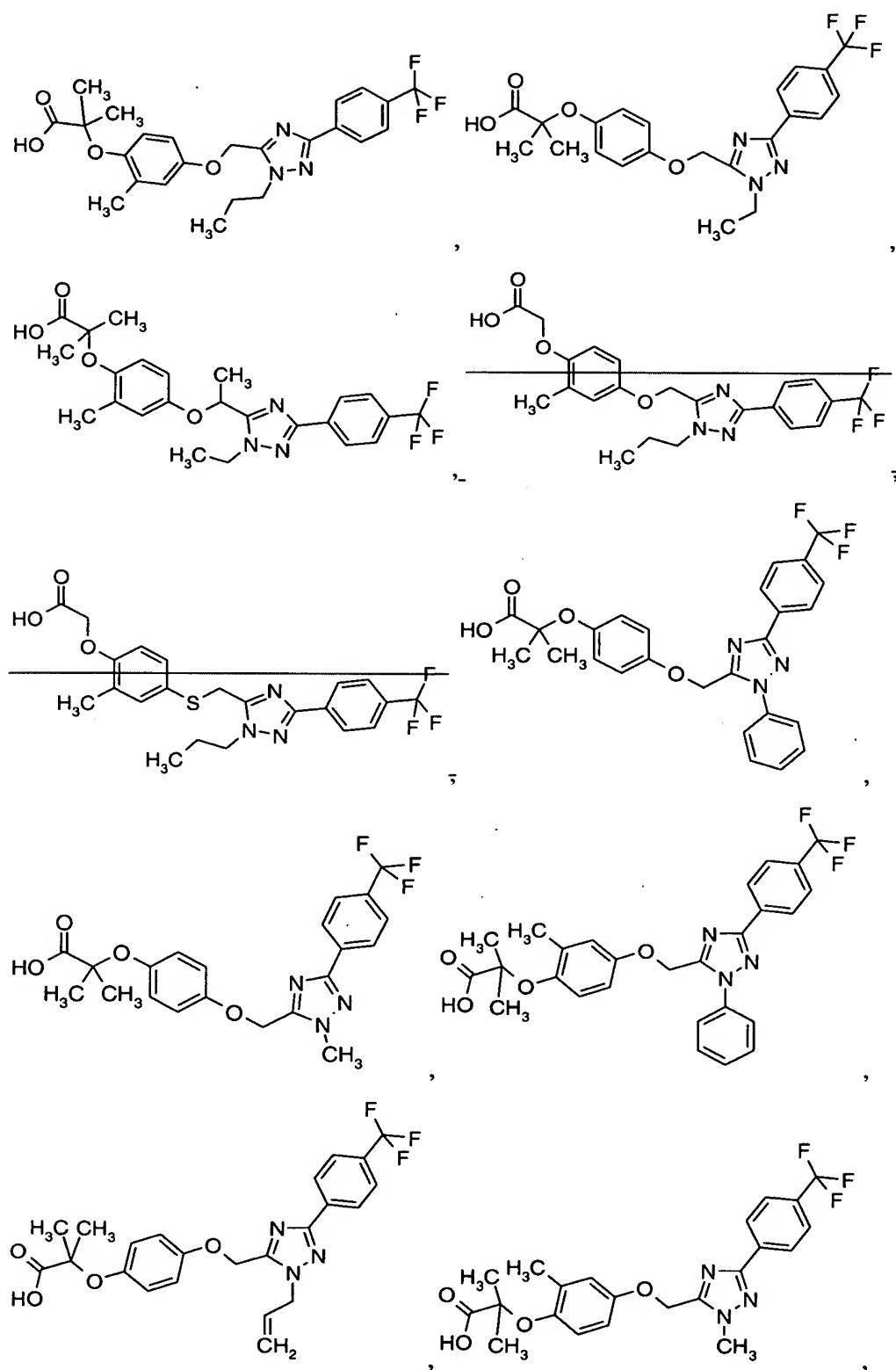
71. (Canceled)

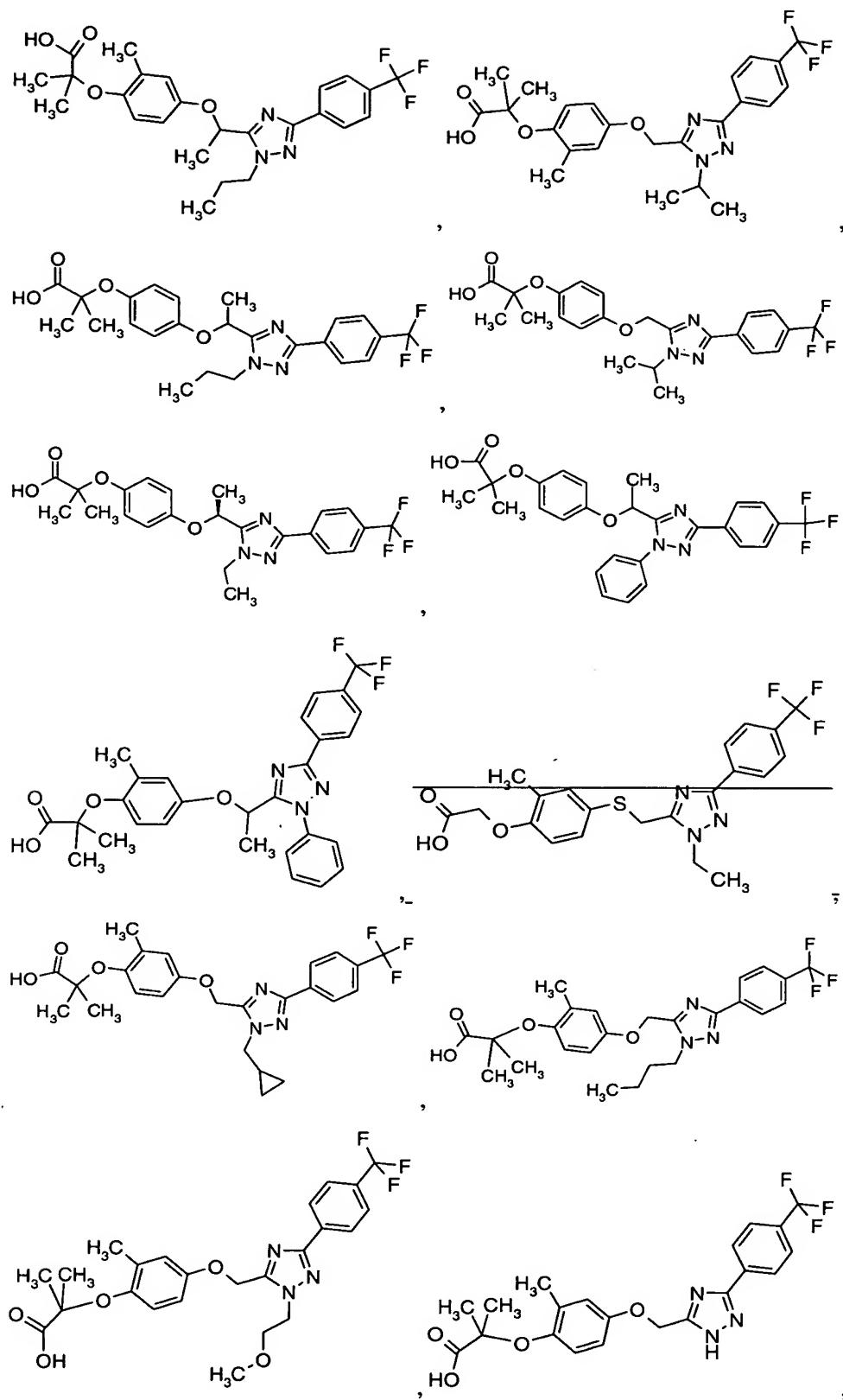
72. (Canceled)

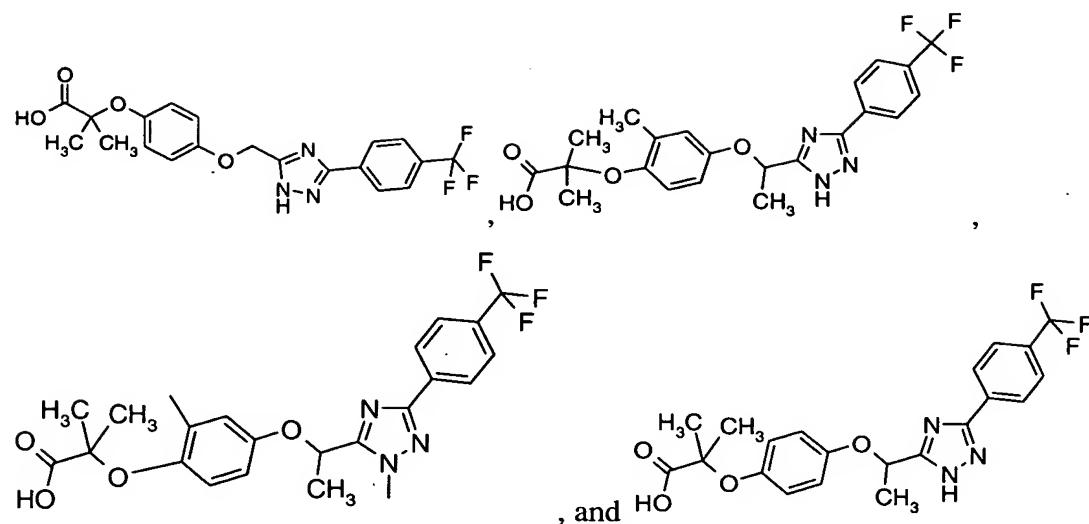
73. (Canceled)

74. (Currently Amended) A compound as claimed by Claim 3 Claim 45 wherein the compound is selected from the group consisting of:



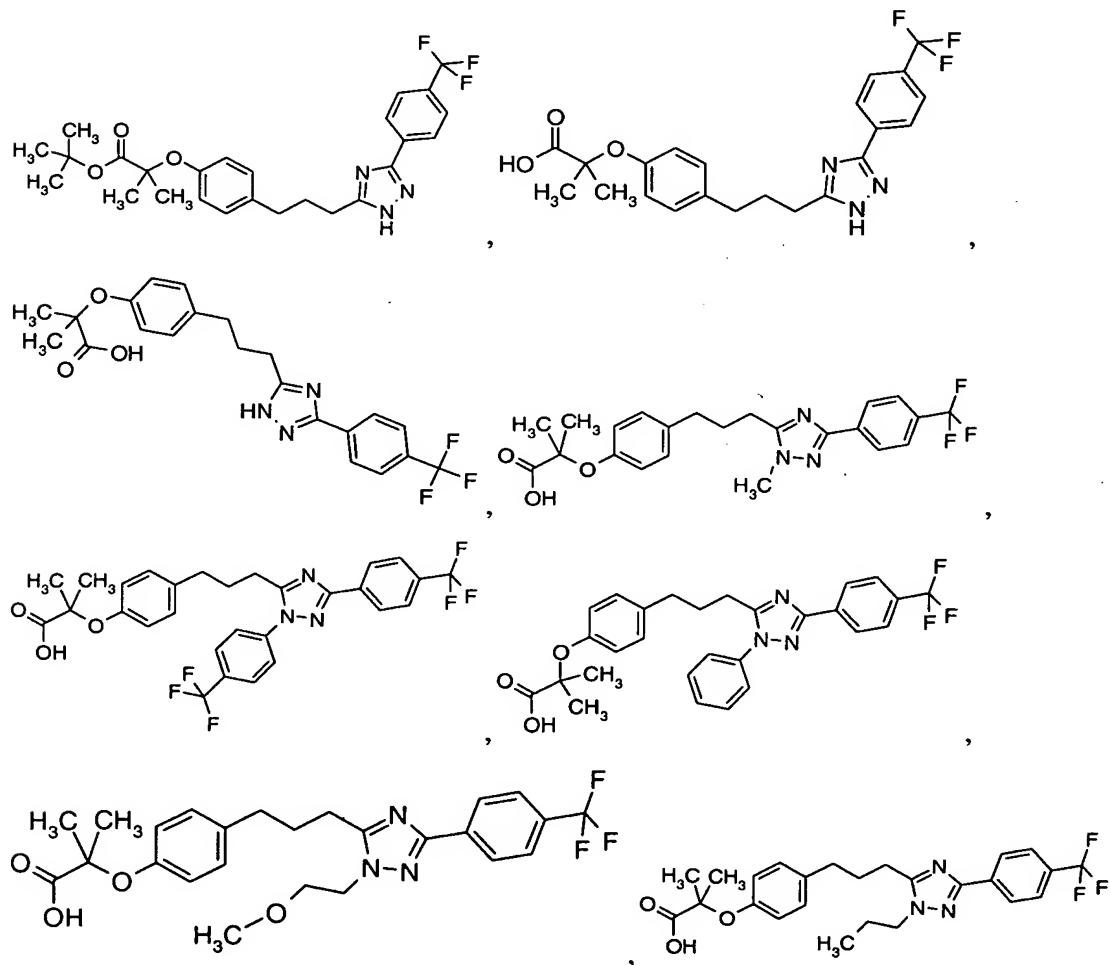


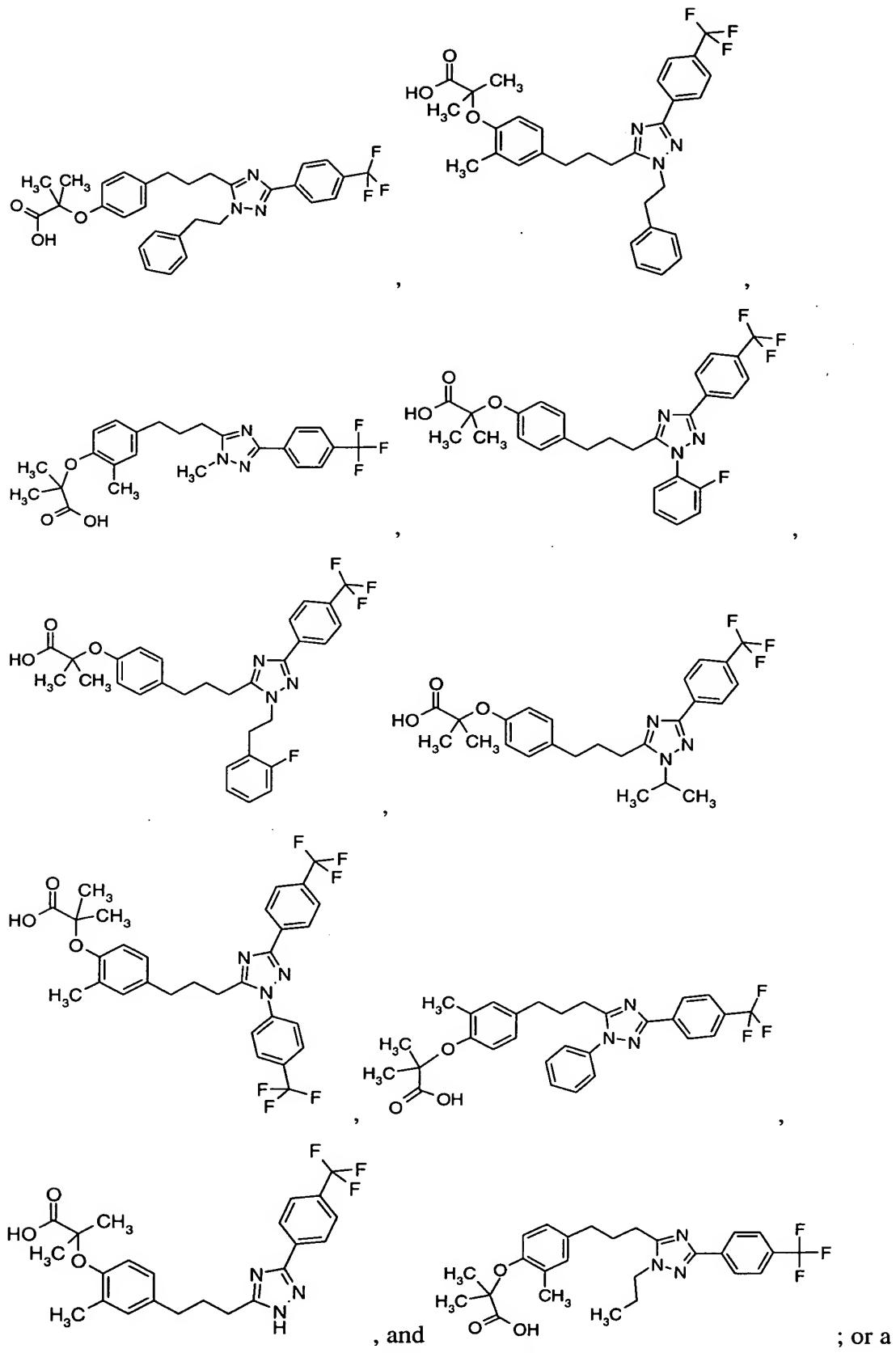




or a pharmaceutically salt, solvate, or hydrate thereof.

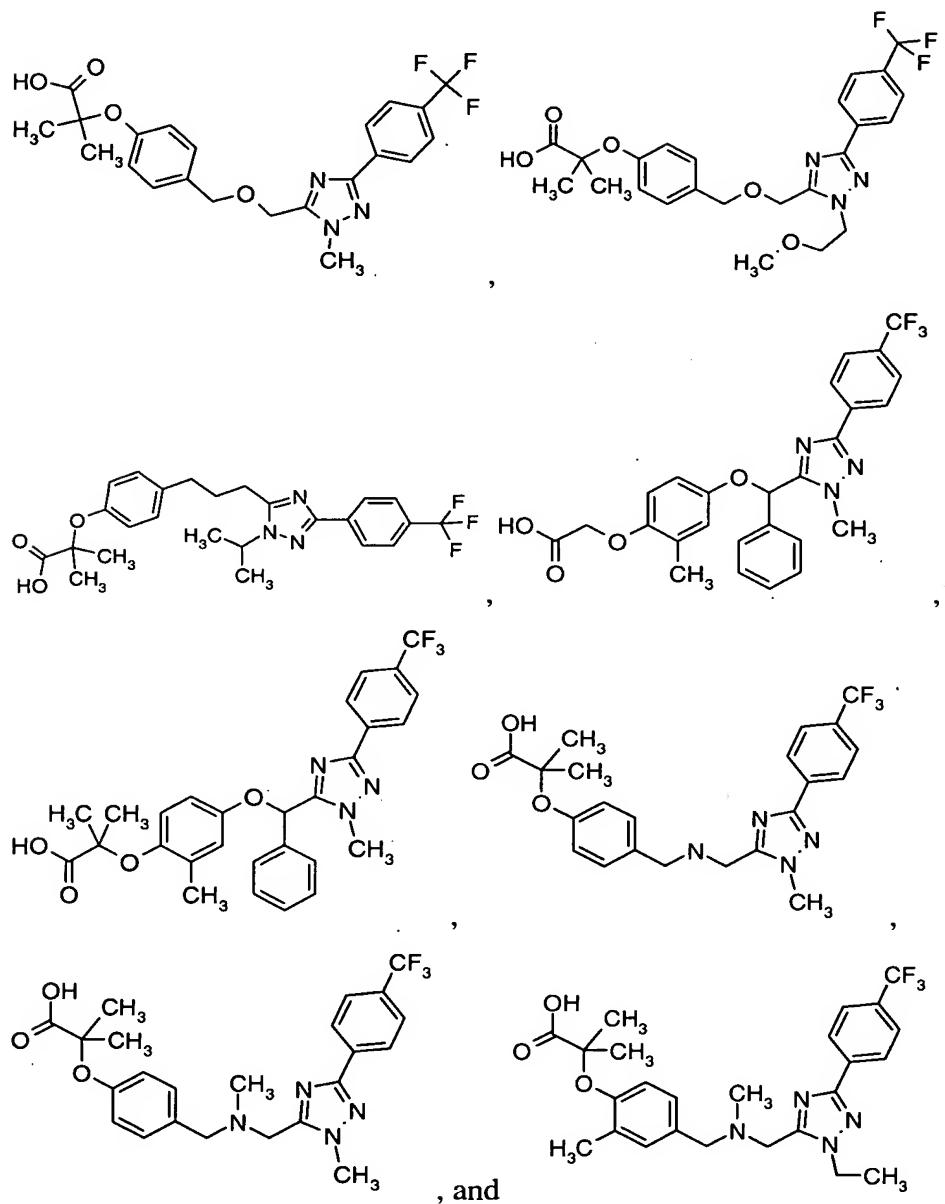
75. (Original) A compound as claimed by Claim 46 wherein the compound is selected from the group consisting of:





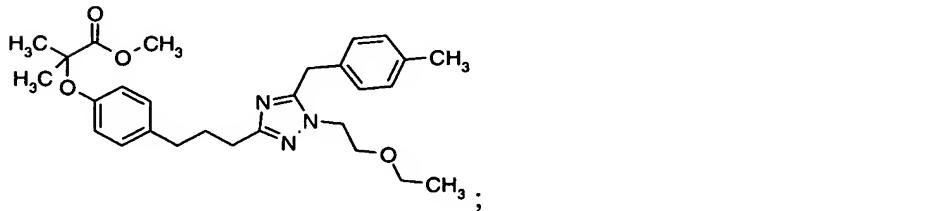
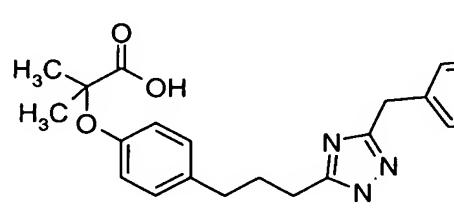
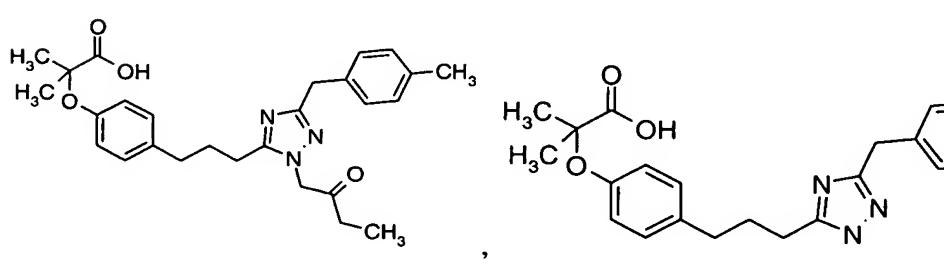
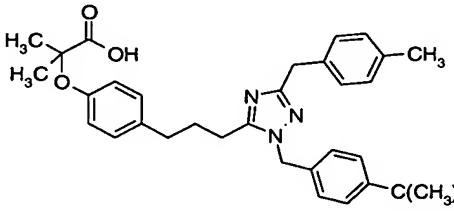
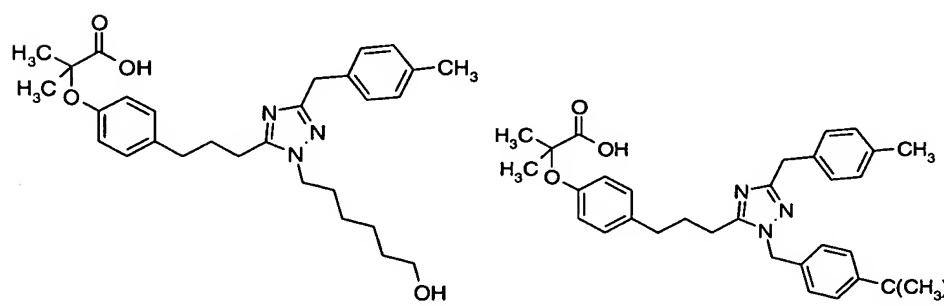
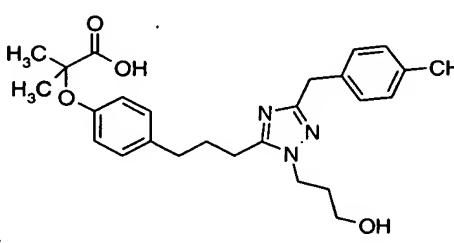
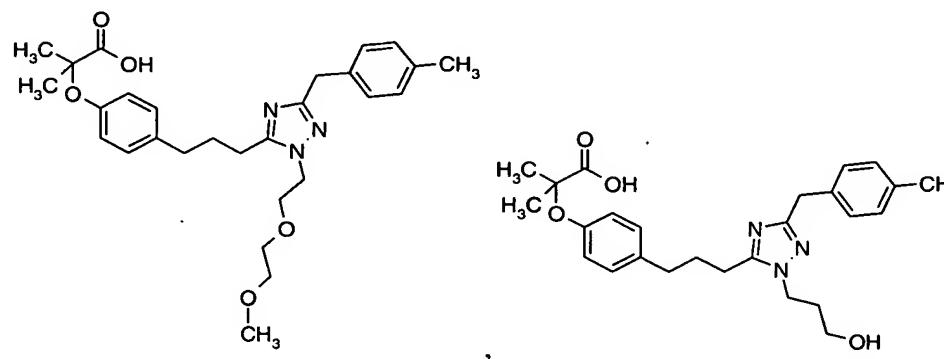
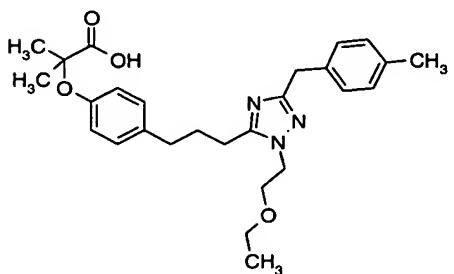
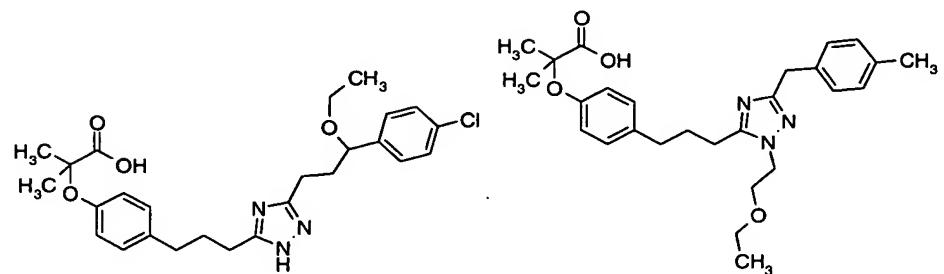
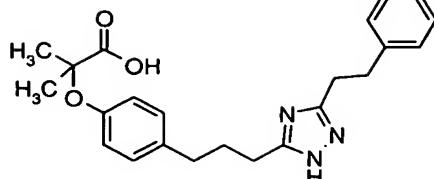
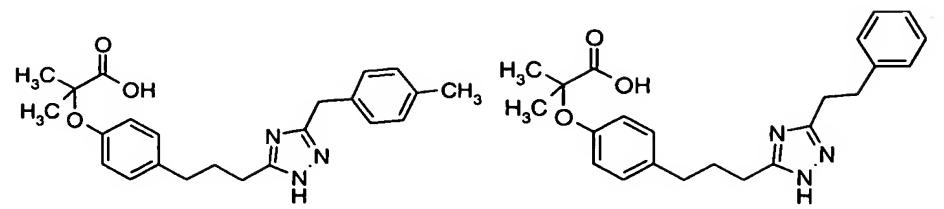
pharmaceutically acceptable salt, solvate, or hydrate thereof.

76. (Original) A compound as claimed by Claim 46 wherein the compound is selected from the group consisting of:

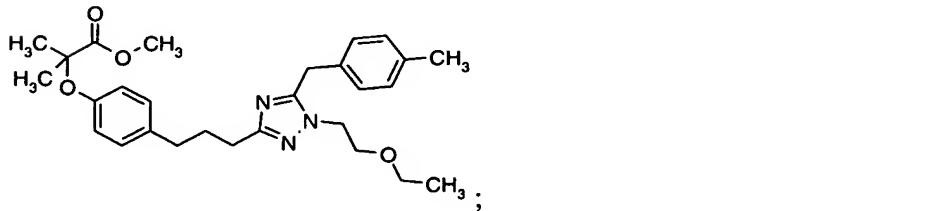


or a pharmaceutically salt, solvate, or hydrate thereof.

77. (Original) A compound as claimed by Claim 48 wherein the compound is selected from the group consisting of:



, and



or a pharmaceutically salt, solvate, or hydrate thereof.

78. (Cancel)

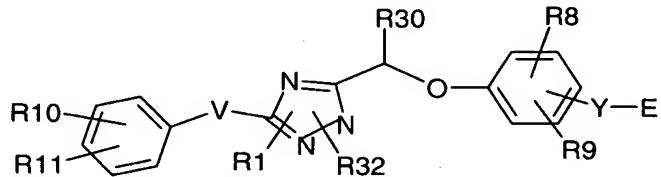
79. (Cancel)

80. (Cancel)

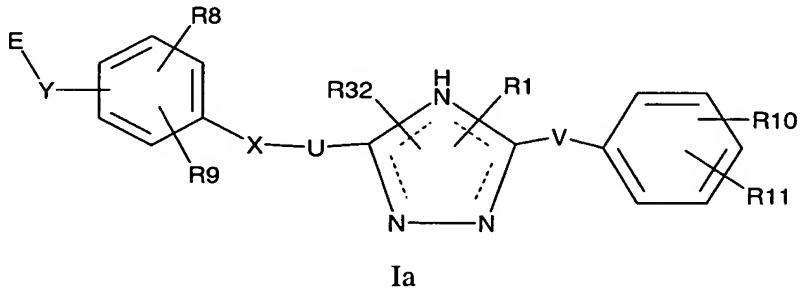
81. (Cancel)

82. (Currently Amended) A pharmaceutical formulation comprising a compound as claimed by Claim 3 ~~any one of Claims 1 through 55, Claims 70 through 81, 83 or 84~~ and at least one pharmaceutically acceptable excipient or carrier.

83. (Currently Amended) A compound as claimed by Claim 3 ~~any one of Claims 1, 2, 3, 8, 12-26, 39, 40, and 43~~ of the structural formula:



84. (Currently amended) A compound as claimed by Claim 3 any one of claims 1, of the Formula Ia:



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

- (a) R1 is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₁-C₈ alkenyl, C₁-C₈ heteroalkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl,

- heteroaryl-C₀₋₄-alkyl, and C_{3-C6} cycloalkylaryl-C₀₋₂-alkyl, and, wherein C_{1-C8} alkyl, C_{1-C8} alkenyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C_{3-C6} cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents independently selected from R1';
- (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_{1-C6} alkyl, C_{1-C6} alkyl-COOR₁₂, C_{1-C6} alkoxy, C_{1-C6} haloalkyl, C_{1-C6} haloalkyloxy, C_{3-C7} cycloalkyl, aryloxy, aryl-C₀₋₄-alkyl, heteroaryl, heterocycloalkyl, C(O)R₁₃, COOR₁₄, OC(O)R₁₅, OS(O)₂R₁₆, N(R₁₇)₂, NR₁₈C(O)R₁₉, NR₂₀SO₂R₂₁, SR₂₂, S(O)R₂₃, S(O)₂R₂₄, and S(O)₂N(R₂₅)₂; R₁₂, R₁₃, R₁₄, R₁₅, R₁₆, R₁₇, R₁₈, R₁₉, R₂₀, R₂₁, R₂₂, R₂₃, R₂₄ and R₂₅ are each independently selected from the group consisting of hydrogen, C_{1-C6} alkyl and aryl;
- (c) V is selected from the group consisting of C_{0-C8} alkyl and C₁₋₄-heteroalkyl;
- (d) X is selected from the group consisting of a single bond, O, S, S(O)₂ and N;
- (e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is substituted with from one to four substituents each independently selected from R₃₀;
- (f) Y is selected from the group consisting of C, O, S, NH, and a single bond;
- (g) E is C(R₃)(R₄)A or A and wherein
- (i) A is selected from the group consisting of carboxyl, tetrazole, C_{1-C6} alkynitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R⁷;
 - (ii) each R⁷ is independently selected from the group consisting of hydrogen, C_{1-C6} haloalkyl, aryl C_{0-C4} alkyl and C_{1-C6} alkyl;
 - (iii) R₃ is selected from the group consisting of hydrogen, C_{1-C5} alkyl, and C_{1-C5} alkoxy; and
 - (iv) R₄ is selected from the group consisting of H, C_{1-C5} alkyl, C_{1-C5} alkoxy, aryloxy, C_{3-C6} cycloalkyl, and aryl C_{0-C4} alkyl, and R₃ and R₄ are optionally combined to form a C_{3-C4} cycloalkyl, and wherein alkyl,

- alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with from one to three substituents each independently selected from R26;
- (h) R8 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, and halo;
 - (i) R9 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, halo, aryl-C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, and OR29, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C₁-C₄ alkyl;
 - (j) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkylenyl, C₁-C₆ alkyl-COOR12'', C₀-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)₂R16', N(R17')₂, NR18'C(O)R19', NR20'SO₂R21', SR22', S(O)R23', S(O)₂R24', and S(O)₂N(R25')₂; and wherein aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three independently selected from R28; and wherein R10 and R11 optionally combine to form a 5 to 6 membered fused bicyclic ring with the phenyl to which they are bound;
 - (k) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;
 - (l) R30 is selected from the group consisting of C₁-C₆ alkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl, and wherein C₁-C₆ alkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;
 - (m) R32 is selected from the group consisting of a bond, hydrogen, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, and C₁-C₆ alkyloxo; and

(n) ---- is optionally a bond to form a double bond at the indicated position.